REVIEW ARTICLE

Ultrasonographic Evaluation of Portal Hypertension and Liver Cirrhosis

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Nowadays, ultrasonography is widely available in medical practice for the evaluation of liver cirrhosis and portal hypertension. Real-time ultrasonography (RTUS) is very convenient and is valuable in the detection of liver cirrhosis by demonstrating liver surface nodularity, splenomegaly and right lobe atrophy. Although RTUS is also utilized in the evaluation of portal hypertension by measuring the dimension of the main portal vein and visualizing the portosystemic collaterals, color Doppler ultrasonography (CDUS) and duplex Doppler ultrasonography (dDU) are undoubtedly superior to RTUS in this respect. With CDUS, the flow direction of the portal system can be clearly demarcated, and the collaterals, especially the gastroesophageal, the paraumbilical, the splenorenal and the gastrorenal veins, can be easily detected. With dDU, the measurement of portal flow velocities has been performed for the last two decades; yet, there is inter-equipment and interobserver variation. However, with the combination of the measurements relating to dimension and flow velocity of the main portal vein and changes in the right hepatic vein waveform, dDU is believed to be of value in the assessment of portal hypertension. In addition, several indices such as the congestion index, the portal hypertension index and the "liver cirrhosis index" have been applied in the evaluation of portal hypertension, with increasing evidence of simplicity and diagnostic accuracy. On the whole, ultrasonography is a modern imaging modality which plays an important role in the first-line diagnosis of liver cirrhosis and portal hypertension, because it is reliable, noninvasive and cost-effective.

KEY WORDS — color Doppler ultrasonography, duplex Doppler ultrasonography, liver cirrhosis, portal hypertension, real-time ultrasonography

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Introduction

Pathologically, fibrosis usually occurs during the course of tissue injury or organ damage. The outcome of chronic hepatitis B and C, which are not uncommon in Taiwan, inevitably results in progressive fibrosis during the subsiding-relapsing cycle [1]. Liver cirrhosis is the final stage. Liver biopsy remains the standard method used in the diagnosis of liver fibrosis/cirrhosis, even though it is invasive and has

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certain risks (3% morbidity and 0.03% mortality) [2,3]. According to the Metavir F score, liver fibrosis is graded into five categories: grade 0, no fibrosis; grade 1, enlarged portal tract without septa; grade 2, enlarged portal tract with rare septa; grade 3, numerous septa without cirrhosis; and grade 4, definite cirrhosis [4]. Portal hypertension is the major clinical manifestation of liver cirrhosis and may lead to fatal complications such as esophageal varices bleeding, ascites, hepatic coma and splenomegaly with severe thrombocytopenia. Hence, the best strategy in the clinical management of liver cirrhosis is early diagnosis and, if possible, to prevent its occurrence and progression.

Imaging Modalities to Evaluate Liver Cirrhosis and Portal Hypertension

Modern imaging modalities, including ultrasonography, endoscopic sonography, computed tomography and magnetic resonance imaging, have been used in the clinical evaluation of liver cirrhosis and portal hypertension [5–12]. Among these modalities, ultrasonography including real-time ultrasound (RTUS), color Doppler ultrasound (CDUS) and duplex Doppler ultrasound (dDU) is the most convenient, cost-effective and noninvasive imaging technique. It is clinically acceptable and reliable with a sensitivity, specificity and accuracy the same as or similar to other modalities [7,12–14].

RTUS in the Diagnosis of Liver Cirrhosis

A nodular liver surface, usually combined with a coarse echo-pattern of liver parenchyma on ultrasonography, is a reliable sign in the detection of liver cirrhosis [7,12,15–17] and can have a diagnostic accuracy of 70% or more [12]. Splenomegaly with a length ≥ 11 cm is another valuable diagnostic sign [12,16,18], with a diagnostic accuracy of about 80%. Right lobe atrophy [19,20], usually with concomitant caudate lobe enlargement [21,22], is also frequently seen in liver cirrhosis. The caudate-right lobe ratio has been found to have an accuracy of 60–80% in detecting cirrhosis [12,23].

Repeatedly relapsed hepatic inflammation, a common course of chronic hepatitis [1,16], leads to progression of liver parenchymal fibrosis and finally to the most severe stage, liver cirrhosis. These induce progressive hepatic morphologic change and, finally, liver shrinkage, resulting in liver surface nodularity [15,20]. The macronodular type of cirrhosis can be easier to detect than the micronodular type [14]. Morphologic changes also include focal atrophy and hypertrophy, which can be due to different mechanisms of portal venous perfusion [20]. Progression of liver fibrosis also results in gradually increased portal venous pressure, leading to progressive splenic and other splanchnic venous congestion. The outcome of the former is splenomegaly [16].

Ultrasonography in the Detection of Portal Hypertension

Theoretically, portal hypertension leads to an increased inner dimension of the main portal vein. However, it has been shown that the main portal vein with a dimension >13 mm in the supine position, as a diagnostic indicator, had a sensitivity of 40% or less [24–26], with an accuracy of around only 60% [12]. Several physiologic factors including a postprandial increment in splanchnic flow, respirophasic change and gravity together with patient positional change may cause size variation in the portal vein and, therefore, make this measurement diagnostically unreliable [24,25].

Severe portal hypertension usually leads to portosystemic collaterals, mainly through the gastroesophageal veins, the paraumbilical vein and the splenorenal or gastrorenal veins [7,12,14,25,27]. These collaterals, except for recanalized paraumbilical veins, are rarely visualized by RTUS [7,13,14] but are easily detected by CDUS [7,13,14,25,27,28], with a sensitivity of 70–83% and a specificity of above 90%. CDUS is also very accurate in the detection of portal flow direction and can determine

hepatopetal, bidirectional and hepatofugal portal flow clearly through color coding. With progression of portal hypertension, the portal flow at first becomes slow. However, this slowdown in portal flow velocity can be very difficult to detect using CDUS, unless there is stagnated and/or bidirectional flow to induce color change. Collateral pathways other than those mentioned above, although infrequent, include the pancreaticoduodenal veins, the retroperitoneal veins, the omental veins, gallbladder varices, and intrapelvic varices [7,14,29,30]. Undergoing transvaginal ultrasonography, pararectal and periadnexal varices can be detected in cirrhotic patients with lower gastrointestinal bleeding [29]. Gallbladder varices, if present, are usually observed by conventional CDUS [30]. In addition, CDUS is especially useful in the evaluation of portal vein thrombosis and cavernous transformation, which can develop in chronic but severe portal hypertension [13,14,31,32].

For two or more decades, dDU was widely utilized for the measurement of portal flow velocity to evaluate portal hypertension in cirrhosis. There is still a lack of standard values for diagnosis, because the interobserver and the inter-equipment variations are so prominent [33,34]. However, with fasted patients in the supine position, dDU may be used by the same observer using the same equipment to monitor and evaluate the differences between healthy and diseased conditions, and to assess the effect of medical treatments for cirrhosis [7]. Under these circumstances, cirrhotic patients without collaterals were shown to have a reduced mean portal velocity [26,35–38], with a sensitivity of 82–83% and a specificity of 80–96%, and a reduced maximum portal velocity, with a sensitivity of 66% and a specificity of 98% [39] or a diagnostic accuracy of 62.2% [12], as compared with healthy subjects. Decreased mean portal velocity was demonstrated to be a result of elevated intrahepatic resistance with an increased hepatic venous pressure gradient [39].

In 1986, Moriyasu et al defined an index of portal hypertension, the congestion index, as the ratio of cross-sectional area to portal flow velocity [40]. This index has been shown to be more sensitive and more specific in the diagnosis of portal hypertension than measurements of portal velocity [41], although it was also found to have a critical limitation in that it needed a very skillful operator [42]. For simplicity, the author set up a new index, the portal hypertension index, calculated as the ratio of the main portal vein dimension (D, mm) at the porta hepatis to the mean portal velocity (Vmean, cm/s) at the same site [26], to detect portal hypertension in an easier way. Both the congestion index and the portal hypertension index were recently demonstrated to be valuable in differentiating between chronic viral hepatitis and compensated early stage cirrhosis [43,44].

Normally, the flow pattern in the hepatic veins is hepatofugal and multiphasic, corresponding with the cardiac cycle, with two antegrade major peaks followed by a small retrograde wave in the early ventricular systolic phase. In patients with cirrhosis, the small retrograde or reverse wave may disappear early and the triphasicity is lost. In end-stage disease, the waveform becomes completely flat [12,45–48]. Observations of hepatic venous Doppler waveforms are usually carried out in the right hepatic vein and/or its branches, and rarely in the left hepatic veins because of the effects of artifacts on cardiac pulsation [45]. Changes in hepatic vein waveform with cirrhosis have been shown to have a high diagnostic accuracy of 76.8% [12]. However, in my own experience, the waveform change may not be so uniform as that measured in different branches of the right hepatic veins in cirrhotic patients.

Endoscopic sonography is a special entity in the detection of portal hypertension with esophagogastric varices, especially for those inpatients with upper gastrointestinal bleeding. Although not so easy and not so sensitive, it could also be used in the observation and measurement of periesophageal veins, perigastric veins, azygos vein, splenic vein, and mesenteric veins. Due to compression of the varices by the water-filled balloon at the endoscopic tip, endoscopic sonography is inferior to conventional endoscopy for visualization of small submucosal varices [5,6,49].

Hemodynamic changes in the hepatic artery observed by CDUS and dDU could play a less important role in the evaluation of liver cirrhosis and portal hypertension [7,12]. However, the postprandial increment in hepatic arterial resistive index is less prominent in cirrhotic patients than in healthy subjects [50]. In addition, Han et al demonstrated that there were increments in the hepatic artery dimension and a decrement in the resistive index and pulsatility index in the hepatic artery of patients with acute alcoholic hepatitis, compared with that in cirrhotic patients [51].

Liver Cirrhosis Index: A New Way to Detect Liver Cirrhosis?

Liver biopsy and measurement of hepatic venous pressure gradient remain the gold standard for the diagnosis of liver cirrhosis with portal hypertension. However, these techniques are not widely utilized in clinical practice owing to the invasiveness of the procedures. As mentioned above, in regard to ultrasonography, decreased portal flow velocity in combination with mild portal vein dilatation and hepatic venous waveform change may be the major hemodynamic abnormalities in cirrhosis. Could there be a simpler indicator to express such a hemodynamic change, or even better, to determine the grade of liver fibrosis? Let us focus on the periphery of the liver parenchyma where the terminal branches of the portal veins perfuse in and the terminal branches of the hepatic veins drain out. As parenchymal fibrosis progresses, the vascular pressure becomes greater and greater. Consequently, the portal venous flow becomes slower, and in contrast, the hepatic venous flow becomes more and more rapid, resulting from the increased surrounding pressure and/or the concomitant formation of micro-porto-hepatic shunts. Should there thus be an increased ratio of the mean hepatic venous flow velocity (HV-Vmean) to the mean portal venous flow velocity (PV-Vmean)? The author did measure the HV-Vmean/PV-Vmean ratio at the vascular terminals of the right lobe of the liver by CDUS/dDU to observe liver cirrhosis. An increased ratio in cirrhotic patients was noted, which was much higher than that in healthy subjects [52]. This ratio may be a new "liver cirrhosis index".

Conclusion

Conventional ultrasonography, as the combination of RTUS, CDUS and dDU, has proved to be very valuable in the assessment of liver cirrhosis and/with portal hypertension. However, there is still a lack of standards for intercommunication between observers and equipment because of prominent variations in the measurements using CDUS and dDU. Hence, we need cooperation, inter-tolerance and open-innovation to resolve this problem and to allow further research and improve clinical practice.

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